



General

Guideline Title

Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline update from the American College of Physicians.

Bibliographic Source(s)

Qaseem A, Barry MJ, Humphrey LL, Forcica MA, Clinical Guidelines Committee of the American College of Physicians. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med.* 2017 Feb 21;166(4):279-90. [140 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Qaseem A, Humphrey LL, Sweet DE, Starkey M, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2012 Feb 7;156(3):218-31. [134 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

May 16, 2017 – [Canagliflozin \(Invokana, Invokamet\)](#) : Based on new data from two large clinical trials, the FDA has concluded that the type 2 diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR) causes an increased risk of leg and foot amputations. FDA is requiring new warnings, including the most prominent Boxed Warning, to be added to the canagliflozin drug labels to describe this risk.

Recommendations

Major Recommendations

Definitions for the overall quality of evidence (high, moderate, low, or insufficient evidence to determine net benefits or risks) and the strength of the recommendations (strong, weak) are provided at the end of the "Major Recommendations" field.

Recommendation 1: The American College of Physicians (ACP) recommends that clinicians prescribe metformin to patients with type 2 diabetes when pharmacologic therapy is needed to improve glycemic control. (Grade: strong recommendation; moderate-quality evidence)

Metformin is effective in reducing glycemic levels, is associated with weight loss and fewer hypoglycemic episodes, and is cheaper than most other pharmacologic agents. Although the evidence was considered low quality, metformin may have an advantage over sulfonylurea monotherapy in terms of cardiovascular mortality. Therefore, unless contraindicated, metformin is the drug of choice for patients with type 2 diabetes, in addition to lifestyle modification.

As defined by the U.S. Food and Drug Administration (FDA), metformin is contraindicated in patients with decreased tissue perfusion or hemodynamic instability, advanced liver disease, alcohol abuse, acute unstable congestive heart failure, or any condition that might lead to lactic acidosis. However, the FDA recently concluded that metformin is safe in patients with mild kidney impairment and in some patients with moderate kidney impairment (but is contraindicated in those with an estimated glomerular filtration rate <30 mL/min/1.73 m²).

Recommendation 2: ACP recommends that clinicians consider adding a sulfonylurea, a thiazolidinedione, a sodium–glucose cotransporter-2 (SGLT-2) inhibitor, or a dipeptidyl peptidase-4 (DPP-4) inhibitor to metformin to improve glycemic control when a second oral therapy is considered. (Grade: weak recommendation; moderate-quality evidence.) ACP recommends that clinicians and patients select among medications after discussing benefits, adverse effects, and costs.

Combination therapies with metformin were more effective than metformin monotherapy in reducing hemoglobin A_{1c} (HbA_{1c}) levels, weight, and blood pressure in patients with type 2 diabetes. This recommendation is graded as weak because of the fine balance between benefits and harms for the various drug combinations. See Table 2 in the original guideline document for a summary of the comparative benefits and harms of metformin combination therapies as well as the adverse effects and cost of each medication. The evidence review did not include therapies combining more than 2 agents. Combination therapies also were associated with an increased risk for adverse effects compared with monotherapy.

Sulfonylureas have been used for many years and are the least expensive oral agent to add to metformin. However, sulfonylureas, both alone and combined with other agents, are associated with an increased risk for mild, moderate, or severe hypoglycemia as well as weight gain. The evidence review did not address medication switching for patients currently taking sulfonylureas. Regarding patients whose glycemic levels are adequately controlled and who do not have adverse effects with sulfonylureas, keeping them on this drug may be reasonable.

The SGLT-2 inhibitors are favored over sulfonylureas as an add-on to metformin therapy in terms of cardiovascular mortality, HbA_{1c}, weight, systolic blood pressure, and heart rate and are favored over DPP-4 inhibitors as an add-on to metformin therapy in terms of weight and systolic blood pressure. As an add-on to metformin therapy, DPP-4 inhibitors are favored over sulfonylureas for long-term all-cause mortality, long-term cardiovascular mortality, and cardiovascular morbidity; over pioglitazone for short-term cardiovascular morbidity; and over sulfonylureas or thiazolidinediones for weight.

Each class of drugs is associated with adverse effects, which are summarized in Table 2 of the original guideline document. The FDA warned that the DPP-4 inhibitors saxagliptin and alogliptin may increase the risk for heart failure, especially in patients who already have heart or kidney disease. The SGLT-2 inhibitors are associated with an increased risk for genital mycotic infections. Sulfonylureas are associated with an increased risk for hypoglycemia.

Although this guideline addresses only oral pharmacologic therapy, patients with persistent hyperglycemia despite oral agents and lifestyle interventions may need insulin therapy.

Definition

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence: Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose-response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Insufficient Evidence to Determine Net Benefits or Risks: When the evidence is insufficient to determine for or against routinely providing a service, the recommendation was graded as "insufficient evidence to determine net benefits or risks." Evidence may be conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Type 2 diabetes mellitus

Guideline Category

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To present the updated evidence regarding the oral pharmacologic treatment of type 2 diabetes and to replace the 2012 American College of Physicians (ACP) guideline on the same topic

Target Population

Adults with type 2 diabetes

Interventions and Practices Considered

1. Metformin (as monotherapy or in combination with one of the agents below)
2. Thiazolidinediones
3. Sulfonylureas
4. Dipeptidyl peptidase-4 (DPP-4) inhibitors
5. Sodium-glucose cotransporter-2 (SGLT-2) inhibitor

Major Outcomes Considered

- Clinical outcomes
 - All-cause mortality
 - Cardiovascular and cerebrovascular morbidity and mortality
 - Incidence of retinopathy, nephropathy, neuropathy
- Intermediate outcomes
 - Hemoglobin A_{1c} (HbA_{1c})

- Weight
- Systolic blood pressure and heart rate
- Adverse effects of treatment
 - Hypoglycemia
 - Gastrointestinal side effects
 - Genital mycotic infections
 - Other safety outcomes

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was conducted by the Agency for Healthcare Research and Quality (AHRQ) Johns Hopkins Evidence-based Practice Center (see the "Availability of Companion Documents" field).

Data Sources and Searches

The reviewers searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials. The search strategy included terms for the diabetes medications of interest and terms for type 2 diabetes. Appendix Table 1 of the systematic review provides the MEDLINE search strategy.

The reviewers ran the search developed for the prior review with the date restrictions of April 2009 through March 2015. They ran an additional search that included the Medical Subject Heading terms and text words for all of the new medications included in this update, without any date restrictions. After completion of the evidence report, reviewers searched MEDLINE through December 2015, and updated their findings where the strength of evidence changed from low or insufficient to moderate or high.

The reviewers hand-searched the reference lists of all newly included articles and relevant systematic reviews. In addition, they searched ClinicalTrials.gov to identify relevant registered trials and reviewed the U.S. Food and Drug Administration (FDA) Web site for any unpublished additional studies relevant to the topic as part of the gray-literature search.

Study Selection

Two reviewers independently screened titles, abstracts, and full-text articles for inclusion and resolved differences through consensus. They included English language studies of nonpregnant adults with type 2 diabetes that evaluated at least 3 months of use of a diabetes medication or drug combination of interest. The reviewers included head-to-head monotherapy comparisons of metformin, thiazolidinediones, sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, and glucagon-like peptide-1 (GLP-1) receptor agonists; comparisons of metformin alone with a metformin-based combination; and comparisons of metformin-based combinations where the second medication was one of the monotherapies described above or a basal or premixed insulin (refer to Appendix Table 2 of the systematic review). They excluded studies that did not specify adjunctive medications. They excluded acarbose because of its infrequent use and the absence of

new key studies that would substantially change the conclusions from the original report.

The reviewers included randomized, controlled trials (RCTs) that evaluated all-cause mortality, macrovascular outcomes, microvascular outcomes, intermediate outcomes, or safety. They also included observational studies that adequately accounted for confounding, although not for the intermediate outcomes.

Number of Source Documents

The reviewers included 204 studies, 116 of which are newly identified, in the updated review (refer to Appendix Figure in the systematic review [see the "Availability of Companion Documents" field]). Eighty-one percent were randomized controlled trials (RCTs). Appendix Table 3 of the systematic review shows the number and design of studies, by outcome.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized, controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence: Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose-response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Insufficient Evidence to Determine Net Benefits or Risks: When the evidence is insufficient to determine for or against routinely providing a service, the recommendation was graded as "insufficient evidence to determine net benefits or risks." Evidence may be conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Description of the Methods Used to Analyze the Evidence

Data Extraction, Quality, and Applicability Assessment

Using standardized forms, reviewers extracted information on the general study and participant characteristics, interventions, comparisons, and the outcome results. A second reviewer confirmed the abstracted data.

Two independent reviewers assessed risk of bias in individual randomized controlled trials (RCTs) by using the criteria of Jadad and colleagues, as in the prior review. They used the Downs and Black tool for assessment of the risk of bias for the nonrandomized trials and observational studies. To assess study applicability, they evaluated whether the study population, interventions, outcomes, and settings were similar to usual care for people with type 2 diabetes in the United States.

Data Synthesis and Analysis

The reviewers created a set of detailed evidence tables. They conducted meta-analyses when data were sufficient (from at least 3 trials) and studies were sufficiently homogenous with respect to key variables (population characteristics, study duration, and medication dosing). When a trial had more than 1 study group, they included in the quantitative pooling the study group with drug doses and study durations most similar to the other studies for that comparison and outcome.

The reviewers pooled the mean difference between groups for continuous outcomes and calculated pooled odds ratios for the dichotomous outcomes using the intention-to-treat denominator. They evaluated the heterogeneity among the trials by using the I^2 statistic. The reviewers generated summary treatment effects with the random-effects model estimated by using the DerSimonian and Laird method in settings of low heterogeneity ($I^2 < 50\%$) and the profile likelihood estimate in settings of high heterogeneity ($I^2 \geq 50\%$).

Grading of the Evidence

Adapting an evidence grading scheme recommended in the Agency for Healthcare Research and Quality (AHRQ) guide for conducting comparative effectiveness reviews, 2 reviewers sequentially graded the studies' limitations, consistency, directness, precision, and potential reporting bias for the evidence on each outcome and comparison. The reviewers graded the evidence separately for RCTs and observational studies. The final evidence grade and conclusion were based on the RCTs and could be strengthened by evidence from observational studies with few study limitations. High strength of evidence indicates that the evidence probably reflects the true effect; moderate strength indicates that further research may change the result; and low strength indicates low confidence that the evidence reflects the true effect, and further research is very likely to change the result. Insufficient evidence indicates that evidence is unavailable or the body of evidence has unacceptable deficiencies, precluding a conclusion.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These recommendations are based on a systematic evidence review sponsored by the Agency for Healthcare Research and Quality (AHRQ) that addressed the following key questions:

Key Question 1

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative effectiveness of the specified monotherapy U.S. Food and Drug Administration (FDA)-approved diabetes medications for the intermediate outcomes of hemoglobin A_{1c} (HbA_{1c}), weight, systolic blood pressure, and heart rate?

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative effectiveness of the specified metformin-based combinations of FDA-approved diabetes medications for the intermediate outcomes of HbA_{1c}, weight, systolic blood pressure, and heart rate?

Key Question 2

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative effectiveness of the specified monotherapy FDA-approved diabetes medications for the long-term clinical outcomes of all-cause mortality, cardiovascular and cerebrovascular morbidity and mortality, retinopathy, nephropathy, and neuropathy?

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative effectiveness of the specified metformin-based combinations of FDA-approved diabetes medications for the long-term clinical outcomes of all-cause mortality, cardiovascular and cerebrovascular morbidity and mortality, retinopathy, nephropathy, and neuropathy?

Key Question 3

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative safety of the specified monotherapy FDA-approved diabetes medications regarding liver injury, lactic acidosis, pancreatitis, hypoglycemia, congestive heart failure, cancer, severe allergic reactions, macular edema or decreased vision, and gastrointestinal side effects; for comparisons including SGLT-2 inhibitors, what is the comparative safety regarding urinary tract infections, impaired renal function, genital mycotic infections, fracture, and volume depletion?

In adults aged 18 years or older with type 2 diabetes mellitus, what is the comparative safety of the specified metformin-based combinations of FDA-approved diabetes medications regarding liver injury, lactic acidosis, pancreatitis, hypoglycemia, congestive heart failure, cancer, severe allergic reactions, macular edema or decreased vision, and gastrointestinal side effects; for comparisons including sodium-glucose cotransporter-2 (SGLT-2) inhibitors, what is the comparative safety regarding urinary tract infections, impaired renal function, genital mycotic infections, fracture, and volume depletion?

Key Question 4

Do the comparative safety and effectiveness of these treatments differ across subgroups defined by the age, sex, race/ethnicity, and body mass index of adults with type 2 diabetes?

This guideline rates the evidence and recommendations by using the American College of Physicians' (ACP's) guideline grading system (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). Details of the guideline development process can be found in the ACP methods paper (see the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak

Quality of Evidence *Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup.	Insufficient evidence to determine net benefits or risks	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline underwent a peer review process through the journal and was posted online for comments from American College of Physicians (ACP) Regents and ACP Governors, who represent physician members at the regional level.

This guideline was approved by the ACP Board of Regents on July 16, 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Clinical Outcomes

Metformin monotherapy was associated with a lower risk for cardiovascular mortality than sulfonylurea monotherapy.

Intermediate Outcomes

Hemoglobin A_{1c} (HbA_{1c})

Most drugs reduced HbA_{1c} to similar levels.

Dipeptidyl peptidase-4 (DPP-4) inhibitors reduced HbA_{1c} levels less than metformin or sulfonylureas.

All combination therapies with metformin were superior to metformin monotherapy.

Weight

Metformin was better than thiazolidinediones, sulfonylureas, or DPP-4 inhibitors for weight.

Combinations of metformin and sodium–glucose cotransporter-2 (SGLT-2) inhibitor agonists reduced

weight more than metformin monotherapy.

Thiazolidinediones and sulfonylureas, either alone or in combination therapy, were associated with worse weight outcomes.

Systolic Blood Pressure

SGLT-2 inhibitors, as monotherapy or combined with metformin, reduced systolic blood pressure compared with metformin monotherapy.

Refer to the original guideline document for comparative benefits of different oral pharmacologic treatments.

Potential Harms

Adverse Effects of Medications

Metformin: increased risk for gastrointestinal side effects

Sulfonylureas: increased risk for hypoglycemia compared with other drugs

Thiazolidinediones: increased risk for heart failure

Sodium–glucose cotransporter-2 (SGLT-2) inhibitors: increased genital mycotic infections

Refer to the original guideline document for comparative harms of different oral pharmacologic treatments.

Contraindications

Contraindications

As defined by the U.S. Food and Drug Administration (FDA), metformin is contraindicated in patients with decreased tissue perfusion or hemodynamic instability, advanced liver disease, alcohol abuse, acute unstable congestive heart failure, or any condition that might lead to lactic acidosis. However, the FDA recently concluded that metformin is safe in patients with mild kidney impairment and in some patients with moderate kidney impairment (but is contraindicated in those with an estimated glomerular filtration rate <30 mL/min/1.73 m²).

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All American College of Physicians (ACP) clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations.
- Insufficient evidence exists for clinical outcomes, including mortality, cardiovascular morbidity, and micro or macrovascular outcomes, for most drugs and drug comparisons. The evidence review did not address whether patients who are already taking sulfonylureas and have stable hemoglobin A_{1c} (HbA_{1c}) levels should switch to another medication. No data exist regarding the best time to add oral therapies to lifestyle modifications.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Qaseem A, Barry MJ, Humphrey LL, Forcica MA, Clinical Guidelines Committee of the American College of Physicians. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med.* 2017 Feb 21;166(4):279-90. [140 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Feb 21

Guideline Developer(s)

American College of Physicians - Medical Specialty Society

Source(s) of Funding

Financial support for the development of this guideline comes exclusively from the American College of Physicians (ACP) operating budget.

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Composition of Group That Authored the Guideline

Authors: Amir Qaseem, MD, PhD, MHA; Michael J. Barry, MD; Linda L. Humphrey, MD, MPH; Mary Ann Forciea, MD

Clinical Guidelines Committee of the American College of Physicians: Mary Ann Forciea, MD (*Chair*); Nick Fitterman, MD (*Vice Chair*); Michael J. Barry, MD; Cynthia Boyd, MD, MPH; Carrie Horwitch, MD, MPH; Linda L. Humphrey, MD, MPH; Alfonso Iorio, MD, PhD; Devan Kansagara, MD, MCR; Scott Manaker, MD, PhD; Robert M. McLean, MD; Sandeep Vijan, MD, MS; Timothy J. Wilt, MD, MPH

Financial Disclosures/Conflicts of Interest

Dr. Barry reports grants, personal fees, and nonfinancial support from Informed Medical Decisions Foundation and Healthwise, both nonprofits, outside the submitted work. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at

www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M16-1860 .

All financial and intellectual disclosures of interest were declared and potential conflicts were discussed and managed. Drs. Boyd, Iorio, and Vijan were recused from voting on this guideline because of active intellectual conflicts. Dr. Manaker was recused from voting on this guideline because of an active indirect financial conflict. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at

www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgic.htm .

Guideline Endorser(s)

American Academy of Family Physicians - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Qaseem A, Humphrey LL, Sweet DE, Starkey M, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2012 Feb 7;156(3):218-31. [134 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [Annals of Internal Medicine Web site](#) .

Availability of Companion Documents

The following are available:

Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, Chu Y, Iyoha E, Segal JB, Bolen S. Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. *Ann Intern Med.* 2016 Jun 7;164(11):740-51.

Available from the [Annals of Internal Medicine Web site](#) .

Bolen S, Tseng E, Hutfless S, Segal JB, Suarez-Cuervo C, Berger Z, Wilson LM, Chu Y, Iyoha E, Maruthur NM. Diabetes medications for adults with type 2 diabetes: an update. Comparative Effectiveness Review No. 173. (Prepared by the Johns Hopkins University Evidence-based Practice Center under Contract No. 290-2012-00007-I.) AHRQ Publication No. 16-EHC013-EF. Rockville (MD): Agency for Healthcare Research and Quality; April 2016. Available from the [Agency for Healthcare Research and Quality \(AHRQ\) Web site](#) .

Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. *Ann Intern Med.* 2010 Aug 3;153(3):194-9. Available from the [Annals of Internal Medicine Web site](#) .

A continuing medical education (CME) activity is available from the [Annals of Internal Medicine Web site](#) .

Patient Resources

The following is available:

Oral pharmacologic treatment of type 2 diabetes mellitus. Summaries for patients. *Ann Intern Med* 2017 Feb 21;166(4):1-18. Available from the [Annals of Internal Medicine Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on March 30, 2012. This summary was updated by ECRI Institute on April 4, 2014 following the U.S. Food and Drug Administration (FDA) advisory on Rosiglitazone-containing Diabetes Medicines. This summary was updated by ECRI Institute on September 15, 2015 following the U.S. Food and Drug Administration (FDA) advisory on DPP-4 Inhibitors for Type 2 Diabetes. This summary was updated by ECRI Institute on April 12, 2016 following the U.S. Food and Drug Administration (FDA) advisory on Diabetes Medications Containing Saxagliptin and Alogliptin. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs. This summary was updated by ECRI Institute on April 6, 2017. This summary was updated by ECRI Institute on July 11, 2017 following the U.S. Food and Drug Administration advisory on Canagliflozin (Invokana, Invokamet).

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse[®] (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the [NGC Inclusion Criteria](#).

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.